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Pulmonary embolism syndrome

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Introduction

Pulmonary embolism is defined as an obstruction of the pulmonary vasculature and is a subset of VTE that represents the third most common cause of vascular disease after acute myocardial infarction and stroke. It is a common complication of deep vein thrombosis (DVT) or the penetration of amniotic fluid into the maternal circulation.

The incidence of PE increases with age. Men typically have a higher overall incidence of VTE compared with women , but women have a higher incidence after age 75. At the age of 45 years, there is a lifetime risk of venous thromboembolism of 8.1% with some patient subsets having even higher life time risk, such as African Americans -11.5%, those that are obese - 10.9%, those identified to be heterozygous for factor V Leiden - 17.1%, or those who have sickle cell disease - 18.2%.

The confirmed PE patients can be categorized and triaged according to the presence or absence of the shock or hypotension., therefore PE can be high, intermediate or low risk.

Risk factors include varicose vein disease of the lower limbs, use of combined oral contraceptives or hormone replacement therapy. It usually occurs through small thrombi that are diffused into the pulmonary capillary bed

Purpose

Differentiated estimation of the pathogenetic mechanisms, manifestations and complications of pulmonary embolism, as well as the argumentation of a pathogenetic treatment to combat the complications with risk for the patients' lives

Material and methods

Relevant articles from PubMed with latest update since 2017 january and a clinical case with pulmonary embolism syndrome and its complications.

Clinical presentation

The clinical presentations of PE are heterogeneous and range from asymptomatic in incidentally discovered small subsegmental embolus to massive saddle embolism to cardiogenic shock and/or sudden death in the context of massive saddle embolism. Typical symptoms and/or signs include pleuritic chest pain, dyspnoea, fever, cough, hemoptysis, and syncope.

Physical examination may reveal tachycardia, tachypnea, fever, and hypoxia, as well as reduced breath sounds or rales, jugular venous distention, and right ventricular (RV) heave.

Diagnostic evaluation

Those with high-clinical suspicion, for example, patients presenting pleuritic chest discomfort and dyspnea who have a history of malignancy and recent immobility that manifest hypoxia, tachycardia, and hypotension and are unstable require a distinct evaluation than those with low-clinical suspicion in whom typical symptoms and/or risk factors are not present.

Basic evaluations often performed in these patients include:

•*ECG* which often, but not always, reveals sinus tachycardia, supraventricular arrhythmias and right axis deviation in 15-25% patients.

•*Chest X-ray (CXR)* which may include enlarged PA (Fleischner sign), regional oligemia (Westermark sign), and Hampton hump (wedge-shaped distal infarct).

• *Clinical prediction rules*, such as Wells score, modified Wells score and Geneva scores.

•*D-dimer test* – a sensitive marker of thrombosis, which is used in low and intermediate clinical probability.

•*CTA* – used in high clinical probability with hypotension ore shock, it has high sensitivity and specificity in detecting PE.

•*VQ scan* is used in situations where CT scan is contraindicated, like pregnancy, acute renal failure, and/or contrast allergy.

•*Cardiac biomarkers*, such as, cardiac troponins and BNP.

Key-words:

Pulmonary embolism, deep vein thrombosis, RV failure, vasoconstriction

Pathophysiology

The apperance of VTE is characterized by Virchow triad, which includes issues affecting endothelial injury, stasis of blood flow, and hypercoagulability. *Endothelial injury* can result from surgery, trauma, venous catheters, and superficial vein thrombosis. *Stasis* can be caused by prolonged immobilization during travel, surgery, obesity, and polycythemia vera, with most emboli developing in the lower extremity veins. *Hypercoagulability* can be either genetic (e.g., factor V Leiden mutation, prothrombin gene mutation, antithrombin III deficiency, protein C, S deficiency, and increased homocysteine levels) or an acquired disorder (e.g., antiphospholipid syndrome, infection, inflammatory conditions, cancer, nephrotic syndrome, smoking, using of hormonal contraceptives, hormone replacement therapy, or pregnancy).

The thrombus lodges in the pulmonary arteries from a DVT and causes immediate mechanical obstruction. The embolism activates the coagulation system, damages the endothelium, stagnate pulmonary blood flow and accordingly initiate secondary pulmonary thrombosis which worsens the mechanical obstruction. Mechanical obstruction of the pulmonary vasculature coupled with a complex interaction between humoral factors from the activated platelets, endothelial effects, reflexes and hypoxia cause pulmonary vasoconstriction that worsens RV afterload. Vasoconstrictors include serotonin, thromboxane, prostaglandins and endothelins, counterbalanced by vasodilators such as nitric oxide and prostacyclins.

Hematogenous thromboembolism increases pulmonary arterial pressure (PAP) more effectively than non-hematogenous material, emphasizing the importance of PE-released vasoconstrictors. Activated platelets and the thrombus mass secrete thromboxane-A2, prostaglandins, adenosine, thrombin, and serotonin which induce platelet aggregation and pulmonary vasoconstriction. Pulmonary endothelial cells inactivate serotonin and certain prostaglandins to maintain homeostasis. Endothelins (ET) are produced by the pulmonary vascular endothelium when it is stimulated by thrombin, endothelial injury and hypoxia. ET target the ETA and ETB receptors in the smooth muscle cells, and pulmonary vasoconstriction is induced by activation of phospholipase C that increases IP3, DAG and intracellular Ca+. ET have been estimated to be in charge of 25% of the PE-induced increase in PVR, but findings are variable. ET also induce bronchoconstriction and release of TxA2 which further potentate the pulmonary vasoconstrictor effect.

Vasoconstriction from PE leads to ventilation–perfusion (VQ) mismatch and resulting hypoxia, which leads to the elevation of PVR and pulmonary artery (PA) pressure. Elevated PA pressure results in the reduction in RV stroke volume and RV dilatation. Elevated RV end-diastolic pressures cause neurohumoral stimulation, increased oxygen demand, and resultant subendocardial hypoperfusion, myocardial ischemia, and subsequent infarction. RV dilatation can lead to RV failure. Progression of RV failure can lead to impairment in left ventricular filling and may result in myocardial ischemia due to inadequate coronary artery filling with the appearance of hypotension, syncope, or sudden death. Hypoxia, elevated alveolar-arterial (A-a) gradient, and hypocapnea are frequently observed in PE.

VQ mismatch, right to left shunt, impaired diffusion, and reduced mixed venous oxygen saturation all togather contribute to hypoxia.

Importantly, not all patients are hypoxemic (32% of PE cases demonstrate PaO2 > 80 mmHg), and that the majority of patients (81%) hyperventilate despite the increased dead space with nearly one-third of patients have normal A-a gradient.

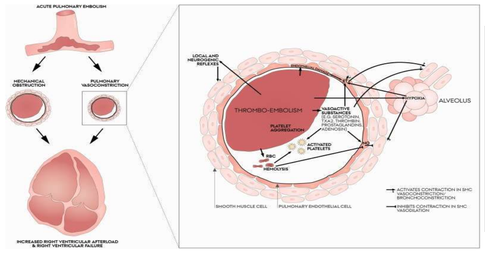

Fig. 1 *On the left*, a schematic pathway showing acute pulmonary embolism (PE) to cause both mechanical obstruction of pulmonary arteries and pulmonary vasoconstriction. Both increases right ventricular (RV) afterload causing acute RV dilatation and interventricular septal shift which have been associated specifically with severe, acute PE. The RV may enter a vicious circle of right ventricular failure, circulatory collapse and death. *On the right*, focus on pulmonary vasoconstriction induced by a pulmonary embolism.

Management

The use of D-dimer testing (a sensitive marker of thrombosis), computed tomographic pulmonary angiography, echocardiography and cardiac biomarkers have facilitated the triage and management of patients with confirmed PE.

The initial treatment should begin with oxygenation and stabilization of the patient. Hereafter the management of PE will continue using direct oral anticoagulants (DOACs) , thrombolytic therapy and catheter-based therapies, with or without fibrinolysis, that have emerged as potential options to treat higher-risk, unstable patients.

Exogenous administration of pulmonary vasodilators in acute pulmonary embolism seems attractive but all come with a risk of systemic vasodilation or worsening of pulmonary ventilation-perfusion mismatch.

Clinical case

A 58 years female with pulmonary cardiomiopathy induced by multiple thromboembolism of pulmonary vessels (massive embolism of left lung), respiratory failure (II-III level) with high risk of assimetric hypertrophic cardiomiopathy and minimal obstruction of left ventricular ejection tract. AHT level III. Mitral failure level II. Cardiac failure level III (NYHA). Right atrium is considerably dilated, but righr ventriculum is weakly modified. Pericardial liquid and high PHT.

Furthermore she has varicose disease of lower limbs (level II) with deep vein thrombosis, which have induced the appearance of pulmonary embolism; also depressive-anxiety syndrome and chronic iron deficiency anemia.

Symptoms: dyspnoea in minimal effort, cough, fever, muco-purulent sputum and hemoptysis, palpitations, general asthenia, high blood pressure, cyanotic teguments, periumbilical cyanosis, face and lower limbs edema, low vesicular murmur and bilateral basal crackling rales.

Special investigations: D-dimer test – negativ, alchalin phosphatase – 143 U/L, dimol test – 1,2 nn.

EKG: sinusal rhythm, sinusal tachycardia, pulmonare P in DII, DIII and AVF, and right atrium hypertrophy. ;

8 years ago has appeared the first access of asphyxia, dyspnoea and severe chest pain. Since then she annually is hospitalized.

During whole hospitalization the signs haven’t improved., but the cardiorespiratory failure has worsen even more, therefore she was connected to oxygen mask. Blood pressure varies between 130-100 mmHg (systolic) si 90-70 mmHg (diastolic).

Treatment: Ca+ antagonists, anticoagulants, antiagregants, diuretics, Ca+ and Fe+ medicaments and O2 therapy.

After hospitalization all the symptoms have been improved for a time.

Results

The clinical case and a lot of relevant scientific articles highlights that in people with untreated deep vein thrombosis, the risk of pulmonary embolism increases significantly and quickly may appear cardiorespiratory complications or a fatal end. Also massive PE can markedly increase physiological dead space and impair CO2 exchange.

Conclusion

PE is a relatively common disorder causing significant morbidity and mortality, induced by right ventricular (RV) failure, which is caused by a combination of mechanical obstruction and pulmonary vasoconstriction, which both increases RV afterload. By combining patient presentation, clinical suspicion, and various scoring systems, diagnosis may be streamlined and a focused treatment can be instituted. Increasingly more physicians possess training and have access to portable ultrasound devices, which may help in the early recognition and treatment of VTE and PE. The increased accuracy of CTA and application of guideline-directed therapies have improved the recognition of PE in patients. Several newer oral anticoagulation drugs are now available and gaining favor among physicians either because they are safer or because they are easier to administrate without periodic monitorization of anticoagulation status.

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